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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/028,245	12/18/2001	Nigel Dunn-Coleman	GC700	2138

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EXAMINER	
RAO, MANJUNATH N	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 06/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/028,245	DUNN-COLEMAN ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 3-21-05, 5-19-05.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 2,4-17,19,20,22-24 and 26 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) 4 and 22-24 is/are allowed.

6)☒ Claim(s) 2,5-17,19,20 and 26 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 2, 4-17, 19-20, 22-24 and 26 are now currently pending in this application and are under consideration.

Applicant's amendments and arguments filed on 3-21-05, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. Specifically, Examiner has withdrawn the previously held rejections of claims 2, 5, 10, 12-17, 19-20 under 35 U.S.C. 112, 1st paragraph because of new matter issues and claims 22, 26 as lacking written description in view of claim amendments. Examiner has also withdrawn the previously held rejections under of claims 6-7 and 8, 9, 11 under 35 U.S.C. 112. 2nd paragraph in view of claim amendments. Objections to specification has been withdrawn in view of amendments.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 5-17, 19-20, 26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide isolated from *T.reesei*, with SEQ ID NO:1 or 4 or a polynucleotide which hybridizes under high stringency conditions to SEQ ID NO:1 or 4, encoding a polypeptide with SEQ ID NO:2 having endoglucanase, (EGVIII), activity and a method of making said endoglucanase, by transforming a host cell with an expression vector comprising the polynucleotide with SEQ ID NO:1 or 4 followed by cultivating the host

cells and recovering the expressed endoglucanase, does not reasonably provide enablement for such a polynucleotide or an expression vector comprising a polynucleotide encoding polypeptides with endoglucanase activity, and 85%, sequence identity to SEQ ID NO:2 (or SEQ ID NO:5?) or polynucleotides encoding polypeptides with encodglucanase activity having 90% or 95% sequence identity with SEQ ID NO:2 or vectors and host cells comprising such polynucleotides, and a method of making said encoded endoglucanase, by transforming a host cell with an expression vector comprising the said polynucleotides followed by cultivating the host cells and recovering the expressed endoglucanase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 2, 5-17, 19-20, 26 are so broad as to encompass any polynucleotide or an expression vector comprising a polynucleotide encoding polypeptide with endoglucanase activity, and having 85% sequence identity to SEQ ID NO:2 (or SEQ ID NO:5?) or polynucleotides encoding polypeptides with encodglucanase activity having 90% or 95% sequence identity with SEQ ID NO:2 or vectors and host cells comprising such polynucleotides, and a method of making said encoded endoglucanase. Claims are also so broad because they

encompass any variant or mutant polynucleotides encoding polypeptides that have 85%, 90%, or 95% sequence identity to SEQ ID NO:2 (or SEQ ID NO:5?). The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claims.

With respect to claims directed to variant polynucleotides encoding polypeptides that have 85%, 90%, or 95% sequence identity to SEQ ID NO:2 (SEQ ID NO:5?), applicants have not taught those skilled in the art as to how to make and select the claimed polynucleotides, which leads to undue experimentation for those skilled in the art. Since the amino acid sequence of a protein encoded by a given polynucleotide, determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence to obtain the desired activity, requires a knowledge of and guidance with regard to which specific amino acids in the protein's sequence, if any, are tolerant to modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only a single endoglucanase, obtained from *T.reesei* and having an amino acid sequence SEQ ID NO:2 . Putting it in simpler terms, the specification is silent regarding the specific amino acids or specific regions in the amino acid sequence of SEQ ID NO:2 that can be modified (by insertion, deletion or substitution) without affecting the endoglucanase activity which could be used to construct variant polynucleotides. Therefore, it would require undue experimentation by a skilled artisan to identify such regions that can be changed and make and use all the claimed variant polynucleotides. The specification is limited to teaching the use of just SEQ ID NO:1 or 4 as

polynucleotides encoding the polypeptide with SEQ ID NO:2. In view of the great breadth of the claim, amount of experimentation required to make the claimed polynucleotides, the lack of a universal method of isolating polynucleotides encoding an endoglucanase from any fungi and lack of guidance regarding where to make the changes in the polypeptide/nucleotide sequences, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495) to make a polynucleotide sequence, the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to make and use the full scope of the polynucleotides encompassed by this claim.

While recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass polynucleotides encoding endoglucanase from any fungi, polynucleotide encompassing any or all modifications and fragments encoding a polypeptide with 85%, 90%, or 95% identity to the SEQ ID NO:2 because the specification does not establish: (A) regions in the polynucleotide structure which may be modified without effecting its activity of encoding a functional

endoglucanase; (B) the general tolerance of said polynucleotide sequence to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any nucleotide in any polynucleotide with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including polynucleotides from any fungi or polynucleotides with an enormous number of modifications to the polynucleotide encoding the amino acid with SEQ ID NO:2 (SEQ ID NOS:1 or 4). The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polynucleotides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the previous Office action, applicants have traversed the above rejection. Applicants argue that section 112 requires nothing more than objective enablement and how such teaching is set forth is of no importance and recite from *In re Marzocchi.* While Examiner has no disagreement with the applicant's conclusion, in the context of the above claims, he maintains that the specification does not provide enablement.

Next, applicants argue as if the rejection was made for lack of written description (see page 9 of remarks). Applicants maintain that companies which develop enzymes are able to

produce and screen thousands of enzymes in a short period of time and robotic systems have been developed. Applicants argue that they have provided assays and that a person of skill in the art can as a matter of routine, sequence and determine homology of any protein with the EGVIII. Examiner respectfully disagrees. While it can be agreed that a person of skill in the art can as a matter of routine sequence a given protein and determine homology of that given protein with another protein/s, claims are not simply drawn to such a limitation. In the instant case, claims are drawn to *making* such variant polynucleotides and testing each one of them for the activity of encoding a polypeptide with endoglucanase activity. Applicants maintain that they disagree with the Examiner and that the specification does teach how to produce variations in nucleotide sequences as well as whether the mutated sequence falls under the scope of the claims, methods of detecting the homologues and methods of determining the endoglucanase activity etc. While that may be so, applicants are silent regarding the guidance for making specific changes that the Examiner has pointed out. The specification lacks specific guidance for making the claimed variants which leads one of skill in the art to undue experimentation.

Applicants have also made an issue of Examiner's comment regarding the reference of Mosimann et al. which they used in their previous response. Applicants argue that Examiner has not provided any reason why a general principle would not be applicable to a specific protein. In response, Examiner asserts that the reason is that the proteins are highly diverse in their structure and function and such broad generalizations cannot be accepted unless there is support that such generalization applies to the specific protein in question. Endoglucanases are a highly important group of enzymes with wide industrial applications. However, Examiner was unable to find even a single reference which used Mosimann's reference to make variants. It is because of

such lack of collateral support that Examiner concluded that Mosimann's reference has any bearing at all in this argument.

Applicants maintain that because explicit examples are not provided regarding every polynucleotide encoding an endoglucanase does not render the present claims unpatentable and that contrary to Examiner's arguments, applicants are not required to describe in detail each and every embodiment of the presently claimed invention and that indeed description of a representative number of species does not require that the applicant describe each and every species. Here again, it is not clear to the Examiner whether applicants are arguing written description or enablement rejection. Examiner has not rejected these claims as not described but they are rejected as not enabled. While the specification may describe the claimed polynucleotides it does not provide enablement for making the same without undue experimentation.

In the next paragraph, applicants indeed argue that specification teaches how to make the endoglucanase and that it was well known prior to the filing of the instant application that molecular modeling could help predict which alterations in the protein would be tolerated, and that the specification is sufficient under 35 U.S.C. 112 1st paragraph. Examiner respectfully disagrees. While it can be agreed that techniques for making variants are available to those skilled in the art, in order to make variants as claimed by the applicants, guidance is required. Such guidance is not provided by the applicants. As previously stated the specification does not establish: regions in the polynucleotide structure which may be modified without effecting its activity of encoding a functional endoglucanase, EGVIII; the general tolerance of said polynucleotide sequence to modification and extent of such tolerance; a rational and predictable

scheme for modifying any nucleotide in any polynucleotide with an expectation of obtaining the desired biological function; and the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Therefore the above rejection is maintained.

Conclusion

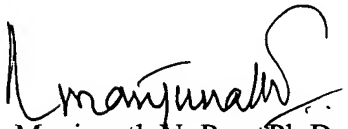
None of the claims except 4, 22-24 are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 571-272-0939. The Examiner can normally be reached on 7.00 a.m. to 3.30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura

Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned is 703-872-9306/9307 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.



Manjunath N. Rao, Ph.D.
Primary Examiner
Art Unit 1652

June 1, 2005